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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/007,779 | 11/30/2001 | Gerardo Castillo | PROTEO.P08 | 1128 |

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EXAMINER

TURNER, SHARON L

ART UNIT PAPER NUMBER

1647

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-------------------------------|---------------------------------|--|
| Office Action Summary | Application No. 10/007,779 | Applicant(s) CASTILLO ET AL. | |
| | Examiner Sharon L. Turner | Art Unit 1647 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-10, 14, 15 and 18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-10, 14, 15 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 4-10, 14-15 and 18 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>5-13-03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed 11-5-04 been entered into the record and has been fully considered.
2. Claims 1-3, 11-13 and 16-17 are canceled. Claims 4-10, 14-15 and 18 are pending.

Election/Restrictions

3. Applicant's election of species d) heparan sulfate identified as reading on claims 4-10, 14-15 and 18 in the reply filed on 11-5-04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4-10 and 14-15 in part to the extent drawn to sulfated macromolecules other than heparan sulfate are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11-5-04.

Claim Objections

4. Claims 4-10 and 14-15 are objected to in part because of the following informalities: The claims are drawn in part to non-elected species, such species being withdrawn as drawn to a non-elected invention. The withdrawal is subject to the non-allowance of the elected invention and generic claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 4 recites the limitation "incubation" in reference to claim 10. However, claim 10 recites co-incubation. There is insufficient clear antecedent basis for this limitation in the claim. Recitation similar to claims 14-15 is suggested, i.e., wherein the step of co-incubation....

8. Claims 6-7 recite the limitation "the molar ratio" in reference to claim 10. However, there is no molar ratio in claim 10 and thus there is insufficient antecedent basis for this limitation in the claim.

9. Claims 7, 9, and 14-15 recite the limitation "about" in reference to the molar ratio, weight ratio, days and temperature of co-incubation. However the metes and bounds of "about" is not determinable by the artisan and the variability deemed to be inclusive of the recitation cannot be discerned.

10. Claims 8-9 recite the limitation "the weight ratio" in reference to claim 10. However, there is no weight ratio in claim 10 and thus there is insufficient antecedent basis for this limitation in the claim.

11. Claims 4-10, 14-15, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

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matter which applicant regards as the invention. Claim 10 recites co-incubation with heparan sulfate but then stipulates the exclusion of EHS perlecan heparan sulfate (an apparent source for the isolation of heparan sulfate). Claim 18 recites co-incubation with EHS perlecan heparan sulfate. The distinction as to the compound to be co-incubated is unclear to the Examiner. Heparan sulfate is that compound regardless of the source of isolation. Applicant's exclusionary recitation appears akin to a "product by process limitation" in the claim, i.e., a limitation as to the source of isolation for the compound. Accordingly the exclusion is null as product by process limitations do not receive the benefit of patentable weight. The process of isolation is not a step within the procedure. Accordingly art is applied to heparan sulfate regardless of source of isolation. If Applicant's are aware of some structural difference between the molecules that offers patentable distinction they should point such out and/or refer to the distinguishing characteristics required within the co-incubation contacting steps. Clarification is required.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 4-10, 14-15 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Snow et al., Neuron 12:219-34, Jan., 1994 (IDS 5-13-03).

Snow et al., teach amyloid plaque infusate components and in vitro incubated beta amyloid for the formation of plaques such as viewed in Figures 2 and 8. In particular the method includes incubation of 10mg/ml beta amyloid 1-40 with heparan sulfate proteoglycan (mouse perlecan 5mg/ml) and EHS HS GAG's 5mg/ml in saline at 37 degrees Celsius for either 1 or 2 week periods, (i.e., 7 or 14 days), see in particular Figure 2 and 8, p. 222 and 230-232, Infusion Reagents and Surgical and Infusion Protocol. The relative weight and molar ratios of AB to perlecan are approximately 1:5, and 1:10-1:13 for example as noted in the surgical and infusion protocol, p. 231. The solutions were noted to be in saline which is "in distilled water" as noted. (Abeta approx. 6kDa and HS approx. 400kDa). Hence the Snow reference is deemed to anticipate claim 4. As recited in claims 5, the sulfated macromolecule of Snow is heparan sulfate and is within the ratios of 1:0.5-1:100 or about 1:5 molar and 1:0.4-1:100 weight or about 1:8 or 1:16 as noted in the surgical infusion protocol, thus meeting the limitations of claims 6-9. As in claims 14-15 the coincubations are at least or about 7 days, 1 week and occur at 37 celsius. Thus, the reference teachings anticipate the claimed invention.

14. Claims 4-10, 14-15 and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Castillo et al., J. of Neurochem., 69:2452-2465, Dec., 1997 (IDS 5-13-03).

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Castillo et al., teach coincubation of amyloid beta peptide 1-40 with heparin or heparin sulfate proteoglycan (perlecan) at a temperature of 37 degrees Celsius for 1 or 2 week periods. The ratios of AB:HS or heparin include molar ratios equivalent to 1:0.5 and 1:100 and weight ratios at 1:1 and 1:100, also inclusive of molar ratio 1:5 and weight ratio 1:8 as disclosed in the solid-phase binding immunoassay studies and thioflavin T fluorometry as disclosed in particular at p. 2454, columns 1-2 and Figures 1-8 and in particular as the assays were performed with various dilutions which correlate in the desired range, see in particular Figures 1-3. Further as in claim 4, the dilutions are noted in Tris-buffered saline at pH 7.0, see for example p. 2454-5, column 2 entitled Analysis of Abeta fibrillogenesis by Thioflavin T fluorometry. As to claim 9, Castillo et al., as set forth above does not specifically teach coincubation of a molar ratio beta amyloid:heparin at a ratio of 1:5 or coincubation of a weight ratio of beta-amyloid:heparan sulfate of 1:8 or 1:16. However, Castillo et al., do teach a range of various dilutions of beta amyloid coincubated with either heparan sulfate (perlecan) or heparin at 10uM based on a mass of 6kDa. (Abeta approx. 6kDa and HS approx. 400kDa). Thus, the artisan would recognize based on the analysis of various concentrations and resultant binding curves as exhibited in Figures 1-8 that a molar ratio of 1:5 A β :heparin and a weight ration of 1:8 A β :heparan sulfate were within the representative ranges for binding and plaque formation as disclosed in Castillo et al., 1997. The sulfated macromolecule is heparan sulfate and in particular EHS perlecan Heparan sulfate GAG chains and thus the reference anticipates claims 5 and 18 explicitly. As noted above in the 112, second paragraph rejection, no patentable

distinction is made between the source of the heparan sulfate, ie., heparan sulfate and EHS perlecan heparan sulfate and thus the exclusion is deemed to be a product by process limitation not receiving patentable weight as to the contacting step with the same product. It is further noted that the method provides for no method steps which distinguish the isolation of the heparan sulfate of the claims. Accordingly, the reference teachings anticipate the claimed invention.

Status of Claims

15. No claims are allowed.
16. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

Sharon L. Turner, Ph.D.
February 14, 2005


SHARON L. TURNER, PH.D.
PATENT EXAMINER
2-14-05